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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,315	O'CONNOR ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant is advised that claims are improperly numbered. Claim 21 has been properly renumbered to claim 20.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2, 4-5, 7-8, and 10-11 drawn to a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting production of the RAD52 protein using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture, classified in class 424, subclass 93.2.

II. Claims 1-2, 4-5, 7, 9, and 10-11 drawn to a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting production of the RAD52 protein using double-stranded RNAi or antisense RNA wherein said cell is ex vivo, classified in class 514, subclass 44.

III. Claims 1, 3, 6-8, and 10-11 drawn to a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture, classified in class 424, subclass 93.2.

IV. Claims 1, 3, 6-7, and 9-11 drawn to a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo, classified in class 514, subclass 44.

V. Claims 12-14 drawn to a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component, classified in class 514, subclass 44.

VI. Claims 12-14 drawn to a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component, classified in class 514, subclass 44.

VII. Claims 15-16 drawn to a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component, classified in class 514, subclass 44.

VIII. Claims 15-16 drawn to a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component, classified in class 514, subclass 44.

IX. Claims 17-19, and 20 drawn to a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro, classified in class 424, subclass 93.2.

X. Claims 17-19, and 20 drawn to a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo, classified in class 514, subclass 44.

Inventions I and II are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. The method of Invention I comprises using the method and cells in vitro wherein the method of Invention II is a method of gene therapy which requires significantly different methods of practice compared to using the method in vitro.

Inventions I and III are distinct. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. The method of Invention I inhibits production of RAD52 protein, the method of Invention III inhibits binding of DNA by RAD52 and requires materially different and separate protocols from the method of Invention I.

Inventions I and IV are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. The method of Invention I inhibits production of RAD52 protein and is carried out in vitro, the method of Invention IV inhibits binding of DNA by RAD52 and is carried out ex vivo requiring materially different and separate protocols from the method of Invention I.

Inventions I and V are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA

wherein said cell is in a cell-line in culture. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention I is a method of promoting retroviral integration, Invention V is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions I and VI are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. Invention I is a method of promoting retroviral integration, Invention VI is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions I and VII are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting

one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention I is a method of promoting retroviral integration, Invention VII is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions I and VIII are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention I is a method of promoting retroviral integration, Invention VIII is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions I and IX are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding

activity in said cell, wherein the cell is in vitro. The method of inhibiting RAD52 in Invention I has materially different distinct and separate protocols from the method of overexpressing RAD52 in a cell in Invention IX.

Inventions I and X are distinct because they are of separate uses. Invention I is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is in a cell-line in culture. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of inhibiting RAD52 in Invention I has materially different distinct and separate protocols from the method of overexpressing RAD52 in a cell in Invention X.

Inventions II and III are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. The method of Invention II comprises using the method and cells ex vivo and is a method of gene therapy wherein the method of Invention III is a method of using the cells in vitro which requires materially different protocols.

Inventions II and IV are distinct. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-

binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. The method of Invention II requires materially different and separate protocols to those of Invention IV.

Inventions II and V are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. The method of Invention II requires materially different and separate protocols to those of Invention V.

Inventions II and VI are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. The method of Invention II requires materially different and separate protocols to those of Invention VI.

Inventions II and VII are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention II is a method of promoting retroviral integration, Invention VII is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions II and VIII are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. The method of Invention II requires materially different and separate protocols to those of Invention VIII.

Inventions II and IX are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell

comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention II requires materially different and separate protocols to those of Invention IX.

Inventions II and X are distinct because they are of separate uses. Invention II is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibition of RAD52 DNA-binding activity using double-stranded RNAi or antisense RNA wherein said cell is ex vivo. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention II requires materially different and separate protocols to those of Invention X.

Inventions III and IV are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. The method of Invention II is to in vitro cell culture, the method of Invention IV can be used a method of gene therapy which requires materially different and separate protocols.

Inventions III and V are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. The method of Invention III requires materially different and separate protocols to those of Invention V.

Inventions III and VI are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. The method of Invention III requires materially different and separate protocols to those of Invention VI.

Inventions III and VII are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention

VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention III is a method of promoting retroviral integration, Invention VII is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions III and VIII are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. The method of Invention III requires materially different and separate protocols to those of Invention VIII.

Inventions III and IX are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing

mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention III requires materially different and separate protocols to those of Invention IX.

Inventions III and X are distinct because they are of separate uses. Invention III is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is in a cell-line in culture. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention III requires materially different and separate protocols to those of Invention X.

Inventions IV and V are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. The method of Invention IV requires materially different and separate protocols to those of Invention V.

Inventions IV and VI are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the

mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. The method of Invention IV requires materially different and separate protocols to those of Invention VI.

Inventions IV and VII are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention IV is a method of promoting retroviral integration, Invention VII is a method of obtaining an agent that promotes retroviral integration and further formulating the agent. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions IV and VIII are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition

comprising at least one additional component. The method of Invention IV requires materially different and separate protocols to those of Invention VIII.

Inventions IV and IX are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention IV requires materially different and separate protocols to those of Invention IX.

Inventions IV and X are distinct because they are of separate uses. Invention IV is a method of promoting integration of a retroviral vector in the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity by inhibiting binding of DNA by RAD52 using a molecule that binds RAD52 protein wherein said cell is ex vivo. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention IV requires materially different and separate protocols to those of Invention X.

Inventions V and VI are distinct. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into

a composition comprising at least one additional component. The method of Invention V requires materially different and separate protocols to obtain an agent that binds RAD52 protein to that of the method of Invention VI to obtain an agent that inhibits RAD52 binding to DNA.

Inventions V and VII are distinct. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention V is a method of obtaining an agent that promotes retroviral integration by binding and inhibiting RAD52 protien, Invention VII is a method of obtaining an agent that promotes retroviral integration by inhibiting RAD52 protein production. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions V and VIII are distinct. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional

component. The method of Invention V may contain materially different and separate protocols to involve a test substance that binds RAD52 protein to that of the ribozyme in Invention VIII.

Inventions V and IX are distinct because they are of separate uses. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention V requires materially different and separate protocols to those of Invention IX.

Inventions V and X are distinct because they are of separate uses. Invention V is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that bind RAD52 protein, and formulating said agent into a composition comprising at least one additional component. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention V requires materially different and separate protocols to those of Invention X.

Inventions VI and VII are distinct. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. Invention VII is a method of

obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention VI is a method of obtaining an agent that promotes retroviral integration by inhibiting RAD52 binding to DNA, Invention VII is a method of obtaining an agent that promotes retroviral integration by inhibiting RAD52 protein production. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions VI and VIII are distinct. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. The method of Invention VI may require separate and materially different protocols to determine a test substance that inhibits RAD52 DNA binding from the method of Invention VIII using ribozymes to specific for a mammalian RAD52 gene sequence.

Inventions VI and IX are distinct because they are of separate uses. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional

component. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention VI requires materially different and separate protocols to those of Invention IX.

Inventions VI and X are distinct because they are of separate uses. Invention VI is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that inhibit RAD52 binding to DNA, and formulating said agent into a composition comprising at least one additional component. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention VI requires materially different and separate protocols to those of Invention X.

Inventions VII and VIII are distinct. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention VIII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention VII is a method of obtaining an agent that promotes retroviral integration by using specific test substances comprising dsRNA or antisense RNA,

Invention VII is a method of obtaining an agent that promotes retroviral integration by using substances comprising a ribozyme. The methods of each invention require materially distinct and separate protocols to use each method.

Inventions VII and IX are distinct because they are of separate uses. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention VII requires materially different and separate protocols to those of Invention IX.

Inventions VII and X are distinct because they are of separate uses. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise dsRNA or antisense RNA wherein said RNA is complementary to a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention VII requires materially different and separate protocols to those of Invention X.

Inventions VIII and IX are distinct because they are of separate uses. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. The method of Invention VIII requires materially different and separate protocols to those of Invention IX.

Inventions VIII and X are distinct because they are of separate uses. Invention VII is a method of obtaining an agent that promotes retroviral integration into the genome of the mammalian cell comprising selecting one or more test substances that comprise a ribozyme specific for a mammalian RAD52 gene sequence, and formulating said agent into a composition comprising at least one additional component. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention VIII requires materially different and separate protocols to those of Invention X.

Inventions IX and X are distinct. Invention IX is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is in vitro. Invention X is a method of inhibiting retroviral integration in a mammalian cell comprising increasing mammalian RAD52 DNA-binding activity in said cell, wherein the cell is ex vivo. The method of Invention IX contains methods

and protocols drawn to cell culture, which requires materially separate and distinct protocols of Invention X which can be used for gene therapy.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required is different among each group, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari Ph.D whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-F 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 1-571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim*** rejected under 35 U.S.C. 103(a) as being unpatentable over *** as applied to claim*** above, and further in view of ***.

Caumont et al. teach that "retroviral integrase is the enzyme which integrates the linear double-stranded DNA copy of the viral RNA genome in the host-cell genome (pg. 503 col. 1 Introduction lines 1-2 bridge col. 2 line 1), and "that two genetic elements are necessary for the integration reaction: (1) the viral gene encoding integrase, and (2) cis-acting sequences (LTRs) located at the ends of the DNA copy (pg. 503 col. 2 parag. 1 lines 2-5). Caumont continues to teach that "in vitro reactions using HIV-1 integrase protein and HIV-1 LTRs have shown that these two elements are also sufficient for integration" (pg. 503 col. 2 parag. 1 lines 6-9), and that

the "integration reaction is an obligatory step in the replicative cycle of the virus" (pg. 502 col. 2 parag. 2 lines 1-2). Caumont continues that the RAD 52 yeast gene is involved in the repair of double-strand breaks (pg. 507 col. 1 parag. 3 lines 4-5), and that transgenic yeast cells comprising a disruption of the RAD 52 gene have an increased lethal effect due to HIV-1 integrase expression compared to wild-type yeast cells (pg. 506 col. 2 parags. 1-2 and fig. 4A). Caumont continues that "the lethal phenotype due to the HIV-1 integrase expression in yeast may be closely related to the HIV-1 integration reaction in infected human cells, and that yeast may be a useful tool to study the HIV-1 integration process" (pg. 503 Abstract lines 19-23).

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